

**The Use of Venous Access Devices in Patients  
Younger than 21 years with Cancer to Improve  
the Ease of Administration of Intravenous  
Therapies**

**CANDIDATE:**

**Dr Martin R Chasen  
Mary Potter Oncology Centre,  
Little Company of Mary Hospital  
Groenkloof, Pretoria**

**STUDENT NO:**

**CHSMAR005**

**SUPERVISOR:**

**Professor R Abratt**

**In partial fulfilment of the requirements for the degree of  
M.Phil. Palliative Medicine in the Faculty of Health Sciences**

**University of Cape Town**

**June 2004**

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

## **ABSTRACT**

### **Background**

Venous access devices (VAD) are implanted routinely in younger patients with cancer in order to administer therapy. The use of these devices is assumed to decrease the anxiety of repeated venepuncture, and to improve safety and convenience of administration of all intravenous therapies needed to treat such patients.

The aims of this dissertation were:

- (a) To review the records of all patients 21 years and younger with cancer who were treated at a single institution
- (b) To examine the complications that occurred due to the VAD.
- (c) To measure the quality of life of those patients at serial intervals and to determine the financial cost of the VAD.

### **Materials and Methods**

There were 51 patients who had 54 VADs inserted. At each visit 18 patients completed a touch screen version of the EORTC QLQ-C30 questionnaire and these results were compared for all visits. The results were divided into 3 time intervals viz before the VAD insertion, at the time of insertion and 53 days thereafter and after 54 days.

### **Results**

The mean and median age of the 51 patients was 17 years and 37 were male. 21 Patients had sarcoma and 21 had a haematological malignancy. The complications encountered were 7 "port fractures", 2 sepsis, 1 each of erosion through skin, tilting of VAD, hemithorax and jugular vein thrombosis. Improvements of symptoms such as fatigue, nausea, appetite and insomnia occurred as time progressed. The functional sub-scales of cognitive, role and social deteriorated at the time of VAD placement.

The cost of a VAD insertion was R9060 and to remove a VAD was R3700.  
The regular maintenance of a port cost R85.16 per flush.

### **Conclusion**

The VAD is a safe, effective way to gain venous access in younger patients with cancer. The initial deterioration in quality of life scores at the time of placement of the VAD was replaced by a definite improvement to above baseline levels as time progressed. Future studies assessing the QOL in adolescents should use an adolescent directed questionnaire.

University of Cape Town

## **ACKNOWLEDGEMENTS**

- **Sister Tasso Swanepoel for her meticulous typing and constructive criticism of the manuscript.**
- **Professor Raymond Abratt who gave honest, scientific advice and was always available as a supervisor.**
- **Mr Mike Greyling who helped me with my statistics and gave me the time of day.**
- **Dr Liz Gwyther who showed initiative to start the palliative care degree in South Africa.**
- **Professor Neil McDonald who continues to inspire and give encouragement.**
- **My beautiful wife Pam and children Orah and Tikvah who make my life worthwhile.**
- **Hakadosh Baruchu (G-d) who has given me life to live and has blessed me with the ability to help others.**

## TABLE OF CONTENTS

<b>Introduction/Background</b>	<b>1</b>
1(i) Orientation, background and motivation	1
(ii) Incidence of Cancer in Adolescence	2
(iii) Prevalence of Malignant Disease in Adolescence	4
(iv) Venous Access Devices (VAD)	5
(a) Types of devices	6
(b) Complications	9
(v) The Impact of Cancer Diagnosis on Quality of Life	11
(vi) Intravenous Therapies	12
<b>Aims and Objectives of this Dissertation</b>	<b>13</b>
<b>Materials and Methods</b>	<b>14</b>
A. VAD	14
B. EORTC QLQ – C30	17
<b>Data Analysis</b>	<b>19</b>
<b>Results</b>	<b>21</b>
Demographic	21
Response to Therapy	22
Survival	22
VAD Complications	24
At the time of Analysis	25
<b>Financial Cost</b>	<b>27</b>
<b>Quality of Life Assessment</b>	<b>28</b>
<b>Quality of Life Parameters – Table II</b>	<b>30</b>

<b>Discussion</b>	<b>31</b>
<b>Conclusion</b>	<b>37</b>
<b>References</b>	<b>38</b>
<b>Appendix I</b>	

EORTC QLQ - C30 (version 3)

## **I INTRODUCTION/BACKGROUND**

### **1(i) Orientation, background and motivation for the study:**

Over the past few decades with the advent of modern oncology, advances in treatment of patients, especially children less than 15 years of age, has been dramatic. This age group has been the main focus of treatment and research and this research has had a well organized structure which has supported and aided in this success. Groups such as International Society of Paediatric Oncology (SIOP) have worked well in order to fully evaluate treatment regimes and study cancer and patient behaviour.

The internationally accepted definition of childhood, which for the purposes of cancer registration is 0-14 years (Robison LL,1997). As an extension of this definition, in the SEER (Surveillance, Epidemiology and End Results) programme of the National Cancer Institute (NCI) in the United States (Ries LAG,1999), adolescence has been assigned to the 15-19 year age bracket. Adolescence has been defined in many ways, but it may be most effectively viewed as the time of transition between childhood and adulthood (Evans M, 1996). The World Health Organization defines adolescents as individuals between 10 and 20 years of age. This definition allows for wide cultural



diversity. In our culture most 10 year olds will be seen as children.

Adolescence can be seen as a continuum of development that encompasses patients from the age of 10 to 23 years, but which will be flexible at either end of his or her own needs and circumstances, and the developmental tasks required by the individual and by society. There are stages in this transition from childhood to adulthood and at the end of this time, adolescents are expected to emerge into adult life with a positive sense of self-worth, an established identity, a comfortable body image and the ability to form relationships with others of the same and opposite sex. A diagnosis of cancer at this critical time is devastating and brings with it many difficulties for the patient including a dramatic effect on his quality of life. His family and friends as well as his health care professional will all encounter the difficulty along with the patient who has cancer diagnosed at this time.

#### **1(ii) Incidence of Cancer in Adolescence**

Within the database of the SEER programme, the annual incidence rates of cancer in the adolescent is at a little more than 200 per million, which is higher than in a younger quintile (Kosary CL, 1995). For the period 1973-1995, the incidence rate in adolescents increased by 30% whilst the rate in childhood rose by 10%. This was mainly due to an increase in adolescents of malignant germ cell and lymphoid neoplasms (Table 1).

Annually about 1500 to 2000 patients in the UK are diagnosed with cancer between the ages of 15 and 25 years (Leonard R, 1995). In the USA the incidence of cancer in the age group 15–19 years is 20 new cases per 100,000 per year. Incidence data from Canada and Australia are similar (Barr R, 1999 & Parkin DM, 1992).

**Cancer in adolescence: age-specific incidence rates**

Table 1

	1975-1979	1980-1984	1985-1989	1990-1994
Testicular germ cell tumors	22.1	26.7	24.9	28.4
Non-Hodgkin's lymphoma	10.7	14.5	14.4	16.3
Ovarian germ cell tumors	7.9	8.3	11.8	13.3
Acute lymphoblastic leukemia	10.8	13.2	12.4	13.0
Osteosarcoma	6.8	8.9	9.7	9.3
Gonadal carcinomas	2.7	2.4	4.3	5.3

(Ries LAG)

1(iii) **Prevalence of Malignant Disease in Adolescent**

The malignant lymphomas, germ cell tumors and brain tumors account for almost 50% of the total, a distribution different from that in children and adults. Acute myeloid leukemia, diffuse large-cell lymphoma are common and amongst soft tissue sarcomas, non-rhabdomyosarcomatous variants predominate.

Gender differences in incidence are obvious with the M:F ratio ranging from a value of more than 2 for ALL to a striking reversal for thyroid carcinoma which occurs in young women. Osteogenic sarcoma has a ratio of 1,6. Ewing sarcoma of 1,8 and soft tissue sarcomas 1,2.

In South Africa the National Cancer Registry is pathology based (Mqoqi N, 1996-1997). The age specific incidence rates per 100,000 indicate the following:

<b><u>Female 10-14 year age group</u></b>		<b><u>For Males 10-14 years</u></b>	
(i) Bone	1,26	Leukemia	1,43
(ii) PSU	0,54	Brain	0,9
(iii) Leukemia	0,72	Hodgkins	0,58

In the 15-19 year age group:

(i) Bone	1,15	Leukemia	1,87
(ii) Leukemia	0,95	Bone	1,63
(iii) Hodgkin's Disease	0,76	PSU	0,9
(iv) Non-Hodgkin's & Brain	0,48 each		

In the 20-24 year age group:

(i) Basal Cell Carcinoma	1,56	Leukemia	1,25
(ii) Cervix	1,91	Bone	1,2
(iii) Breast	0,93	PSU	1

PSU = Primary Site Unknown

This report is at variance with what is reported in world literature but the accuracy in the reporting is questionable as the registry relies on the different laboratories to report all cases. These results, therefore, are the outcome of incomplete ascertainment and emphasize the need for a complete registry.

1(iv) **Venous Access Devices (VAD)**

The Oncologist faced with the clinical problem of drawing blood and administering chemotherapy or the palliative care physician who may need to draw blood, administer antibiotics, deliver fluid and nutritional support and at times administer analgesics has three choices to choose from when the patient will need treatment over a protracted time : a) Rely on peripheral veni-puncture in the face of ever deteriorating peripheral veins.

b) Insert a form of Hickman-Broviac catheter which emerges through the skin and can be left in-situ for the medium term. c) Insert a totally implantable venous access device (VAD) or port to which is attached a central venous catheter.

The VAD can minimize the discomfort of: i) Repeated veni-puncture, ii) Venous thrombosis and thrombo-phlebitis caused by repeated veni-puncture, iii) Maintain patient mobility and allow him the use of both hands during treatment, iv) Minimize hospital stay. VADs therefore can improve the quality of life in patients with cancer that need repeated intravenous procedures during their illness.

(a) Types of Devices

A. Catheters

In all indwelling catheters used for prolonged central venous access, the proximal capped portion exits from the subcutaneous tunnel on the chest or abdominal wall while the distal tip is indwelling in a central vein (Goodman MS, 1985 & Broviac JW, 1973).

- i) Silicone elastomer catheters with a simple opening at the distal tip include a variety of peripherally inserted central lines viz the Hickman-Broviac(Hickman RO,1979, & Anderson KM, 1992) catheters and Groshong tip catheter. These catheters can be

tunneled under the skin and have a Dacron cuff which is inserted in the subcutaneous tissue just above the exit site.

- ii) Peripherally inserted central catheters (PICC) (James L, 1993 & Banton J, 1999). Advantages include ease of insertion and low risk of serious complications. If maintained properly these lines can last as long as one year and can be used for chemotherapy (Niederhuber JE, 1982) or total parenteral nutrition (Alhimyary A, 1996).

#### **B. Implanted Devices**

Since their introduction, implantable ports have become popular with patients and clinicians alike (Niederhuber JE, 1982). These devices are constructed from a variety of materials including titanium and plastic and can be made compatible with magnetic resonance imaging (MRI) and computed tomography (Ross MN, 1988). The general design includes a compressed silicone diaphragm which can withstand multiple punctures with a Huber needle. These ports are inserted in the operating room.

The port housing is placed in a subcutaneous pocket on the chest wall. The housing is anchored to the underlying fascia by several interrupted sutures. Improvements in the port design have allowed for the construction of a very low profile, small device that can be implanted. Comparisons between these devices, standard Port-o-Caths and external catheters have shown

that both the Port-o-Cath and PAS-port have a reduced incidence of infectious complications when compared to external catheters (Sharpe PC, 1994). Whilst one retrospective study noted no difference in infection rates between Hickman-Broviac catheters and ports, three prospective non-randomized studies indicated a significantly lower complication rate for the ports than catheters especially in younger children (Mirro J, 1990 & Wurzel CL, 1988 & Lucas AB, 1992).

(b) Complications

The complications associated with VAD can be divided into:

1. Those occurring during the placement of the device, such as Arterial Puncture, Cardiac Arrhythmia, Cardiopulmonary arrest, Pneumothorax and incorrect placement of catheter. In a published series undertaken (Decker MD, 1988), the incidence rate of the above complications were 5.2%,1.6%,0.1%,0.5% respectively.
2. Damage to the external segment of the catheter can occur due to repeated clamping of the external connection. Cuts made by scissors mistaken for clamps have been performed.
3. The VAD may "flip" within the pocket because of excessive arm movement or because of manipulation by the patient.
4. Phlebitis and Infiltration. These are uncommon complications associated with properly positioned centrally placed VADs, but are commonly seen with peripherally positioned catheters.
5. Infections. The incidence of infectious complications varies depending on the type of device use. Overall the incidence of catheter associated infections is 1-2 per 1000 days of patient use (Decker MD, 1988). Exit site and tunnel infections are caused by bacteria of which most will respond to antibiotics alone and /or catheter removal. Most are caused by S.epidermis and S aureus. Other organisms include Streptococcus sp and Gram negative rods namely Pseudomonas and Xanthomonas. Fungal infections mainly Candida spp and Aspergillus spp are also well known pathogens (Decker MD, 1988).
6. Hemorrhage. In patients with known thrombocytopenia and also in patients with Disseminated Intravascular Coagulopathy post operative bleeding does occur.



7. **Thrombosis.** Clot formation can occur in the catheter itself or in one of the major vessels of the upper extremity. The thrombosis usually results from failure to follow standard flush procedures. Thromboses were seen in 16% of implanted ports (Press OW, 1984).
8. **Vesicant Drug Extravasation.** It is unusual for a spontaneous leak to form in a large bore catheter, but an attempt to irrigate an occluded catheter with a small syringe can cause a rupture, through which drug can extravasate (Goodman MS, 1985). Occlusion of the catheter tip by a fibrin sheath may force the drug back up the sheath and through the exit site of the catheter (Bottino J, 1979). Leaks may occur if the catheter is disconnected from the reservoir or if the catheter is punctured by mistake by the Huber Needle. In addition outpatients using a port for continuous infusion chemotherapy can suffer drug extravasation if the Huber needle dislodges from the septum (Lucas AB, 1992).

**1(v) The Impact of Cancer Diagnosis on Quality of Life (QOL)**

What is quality of life? Conceptually, QOL is a vague term and most people would agree that QOL is not a unitary concept, but a complex amalgam of satisfactory functioning in essentially four core or primary domains, viz. psychological, b) social, c) occupational, d) physical.

Most items contributing to well-being and life's quality can be listed within one or other of these domains and there is obviously considerable overlap. One feature about good health i.e. relating to the physical domain of QOL is that it is noticed more by its absence than by its presence. In adolescents with cancer, having to be isolated from peers and society by having a disease that makes them different and having to be treated separately is often devastating. In addition, many of the adverse effects of therapy can be overwhelming to an adolescent's self-image, which is often tenuous under the best of circumstances (Woo SY, 1983). Weight gain, alopecia, acne, stunted growth, and mutilating surgery to the face and extremities are examples of adverse consequences that can be devastating to an adolescent's self-image. Repeated venepuncture with needles in order to draw blood and/or administer therapy is a constant source of anxiety and pain for adolescent patients. Other challenges include the time away from friends, school, work, and community that therapy requires and the financial hardships that occur at an age when economic independence from family is

an objective. Although cancer and other chronic diseases in younger and older patients have been shown to increase cohesion among families of affected persons, survivors of cancer during adolescence actually report lower levels of family cohesion than healthy adolescents and their families (Festa RS, 1992). The knowledge of having a life-threatening disease can seriously impair the quality of life of patients. This occurs in individuals who have a good understanding of the implications of the disease and treatment, but is notably worse in those with a poor comprehension of cancer and its treatment.

1(vi) **Intravenous Therapies**

The complex management of the patient with cancer frequently relies on the ability to deliver a variety of intravenous agents over a prolonged period. Chemotherapy, blood and/or blood products, total parenteral nutrition and analgesics may all be required alone or in combination. All require secure access to the circulation as does venous sampling which in such patients is a frequent procedure. Extravasation of chemotherapy agents into the tissues can result in massive tissue destruction even if recognized and treated early. Secondly the veins of the upper limbs are quickly rendered inaccessible by repeated use and the fragility of some veins is the cause of serious local necrosis and tissue destruction.

## **AIMS AND OBJECTIVES OF THIS DISSERTATION**

1.

(i) To retrospectively review the records of patients 21 years and younger at the time of initial treatment that had been seen and treated at the Mary Potter Oncology Center who had a venous access device inserted to aid in their therapy.

(ii) To note the specific complications occurring due to the VAD.

(iii) To evaluate the data of those patients with a VAD who completed the EORTC QLQ –C30 (a quality of life questionnaire) during the course of their cancer.

2. To determine the average financial cost of VAD in patients with cancer with specific reference to: 1) hospital costs to insert the port. 2) additional costs associated with complications. 3) day to day costs.

## **MATERIALS AND METHODS**

All patients were seen and treated at the Mary Potter Oncology Centre in Pretoria by the four resident medical oncologists. The records of those patients who were 21 years and younger at the time of the first consultation, between May 1999 and November 2003, were reviewed. All patients had a VAD inserted prior to chemotherapy administration.

### **A. VAD**

Intravenous access was obtained using a VAD in 51 patients. Three patients had 2 VADs inserted. Various totally implantable titanium venous access port systems were used with a silicone rubber catheter (OD 2.8 mm and ID 1.0 mm). The implantation procedure required the use of a no. 7 French peel-away introducer; a modified Seldinger technique was used for cannulation of the subclavian vein. VADs were implanted under general anaesthesia by one of four surgeons who had agreed to follow a standardized implantation procedure (Strum S, McDermed J, 1986).

### **Materials used for VAD**

Standard sets of supplies for VAD accessing included two sterile towels, one alcohol swab, three povidone-iodine swabs, one pair of sterile gloves, one 20 ml syringe, one Huber needle, two 21-gauge needles, 100 U/ml heparin solution for anticoagulating the VAD reservoir, and one vial of sterile

0.9% saline for flushing the VAD reservoir and catheter. VAD phlebotomy required one additional 10 ml syringe for discard and one additional 20 ml syringe for the blood sample. Treatments that were administered through these devices included:

1. All chemotherapy – the different chemo-therapeutic regimes given were according to specific internationally acceptable protocols and included 2, 3 or more drugs. The main drugs used for these patients were:
  - (i) Doxorubicin and other anthracycline derivatives
  - (ii) Cisplatinum and Carboplatinum
  - (iii) Cyclophosphamide and Iphosphamide/Mesnum-alkylating agents
  - (iv) Vincristine, Vinblastine – Vinca alkaloids
  - (v) Etoposide
  - (vi) Actinomycin-D.
2. Additional fluid therapy. Certain chemo-therapeutic drugs require the additional administration of intravenous fluid in order to minimize organ damage e.g. pre- and post-hydration fluid given concurrently with Cisplatinum. These fluids are given over a few hours and are a vital part of therapy.
3. Supportive drugs such as (i) anti-nauseants including 5HT<sub>3</sub> blockers such as Ondansetron, major tranquilizers such as Chlorpromazine.  
(ii) Corticosteroids such as methyl-prednisolone and Dexamethazone are given intravenously in order to prevent nausea and vomiting.

These are given prior to initiation of the chemotherapy and at regular intervals during the specific treatments. As most chemotherapy drugs, and especially these used to treat the diseases seen in younger patients, are highly emetogenic venous access is paramount for administration of anti-nauseants.

4. Blood and platelet transfusions. These are usually needed at some stage during the course of therapy as patients may become anaemic or thrombocytopenic. This may be due to the effects of the cancer and of the treatment thereof.
5. Antibiotics. These may be required if the patient develops infection as a result of neutropenia caused by the chemotherapy. If the infection is severe, hospitalization in isolation wards is necessary and prolonged intravenous antibiotics may be required to combat infection.
6. Total parenteral nutrition (TPN). Mucositis also may result from the chemotherapy. This can prevent adequate oral fluid and food intake. In order to treat this complication, TPN is given usually in the hospital setting and it too may require prolonged administration.
7. Intravenous hydration in the terminal phase of the patient's life. Many patients' families insist that patients receive hydration during the final

phase of their lives. Having a VAD facilitates the administration of fluid and has the advantage that this can be done at home. Other drugs used during this phase can also be administered intravenously such as anti-nauseants, analgesics, anti-convulsants, anxiolytics and major tranquilizers.

B. The EORTC QLQ-C30 (See Appendix 1) is a 30 item instrument composed of multi-item scales and single items that reflect the multidimensionality of the quality-of-life construct (QOL) (Aaronson NK, Ahmedzar S, 1993). It incorporates five functional scales (physical, role, cognitive, emotional and social) three symptom scales (fatigue, pain, nausea and vomiting) and a global health and quality-of-life scale. The remaining single items assess additional symptoms commonly reported by cancer patients (dyspnoea, appetite loss, sleep disturbance, constipation and diarrhoea) as well as the perceived financial impact of the disease and treatment. The questions are formatted with either yes or no answers, or by using four answer categories that range from 1, not at all, to 4, very much. The two questions on general health and global QOL are answered on a numbered visual analog scale from 1 to 7. The questionnaire has been tested in over 12 countries and has demonstrated high validity in different cancer patient populations (Ringdal GI, 1993).



18 Patients completed a Quality of Life questionnaire at each visit during the time period that they received their chemotherapy. This was usually every 3-4 weeks. A validated 'computer touch screen' version installed at the Mary Potter Oncology Centre was used by the patients. All 18 patients completed the questionnaire without any assistance. The time taken to complete such a questionnaire is between 3 and 5 minutes. All data is electronically stored and can be displayed and compared on the screen according to dates of visits.

## **DATA ANALYSIS**

Statistical analysis was conducted using SAS<sup>®1</sup> system (Version 9.1):

- To determine mean and median survival time estimates, the Kaplan-Meier life table estimates were used (Kaplan-Meier, 1958).
- To explore the differences in quality of life determinants over 3 points in time, the repeated measures ANOVA (Analysis of Variance) was used (Stuart A, 1991).

The 3 points in time relating to the port insertion were:

- (i) Before the insertion of the port (time 1).
- (ii) From time of port insertion up to and including 53 days thereafter (time 2).
- (iii) Anytime after 54 days (time 3).

The scales of the EORTC-QLQ-C30 served as dependent groups and points of time served as independent variables.

<sup>1</sup> SAS is a registered trademark of the SAS Institute

In order to see if an observed difference or relationship reflects the real pattern rather than just a chance anomaly a statistical hypothesis test is performed. Two hypotheses are formulated, the first called the null hypothesis which states that there is no real relationship or difference. The second called the alternate hypothesis, reflects the possible ways in which the null hypothesis could be false. To assess the evidence for the alternatives, a test statistic, which reflects the degree to which the sample results tend towards the alternative hypothesis, is calculated. This determines a probability, called the p-value, which is the probability that the observed findings would occur if the null hypothesis were true. If this is unlikely (usually set at less than 1 in 20 possibility that the observed finding could have occurred by chance), the alternative hypothesis is accepted.

## **RESULTS**

### **Demographic:**

- (i) There were 51 patients who had 54 ports inserted. 37 Patients were male.
- (ii) Their mean and median age was 17 years (9-23 years).  
34 Patients were still alive at time of analysis.
- (iii) The spread of diseases of the group were as follows:

	<b><u>Disease</u></b>	<b><u>Patients</u></b>
1.	Sarcoma/PNET patients	21
2.	Lymphoma	13
3.	Leukemia	8
4.	Medulloblastoma	2
5.	Aplastic Anaemia	2
6.	Testis Carcinoma	1
7.	Dysgerminoma	1
8.	Melanoma	1
9.	Nasopharynx	1
10.	Kidney Cancer	1

(iv) **Response to Therapy**

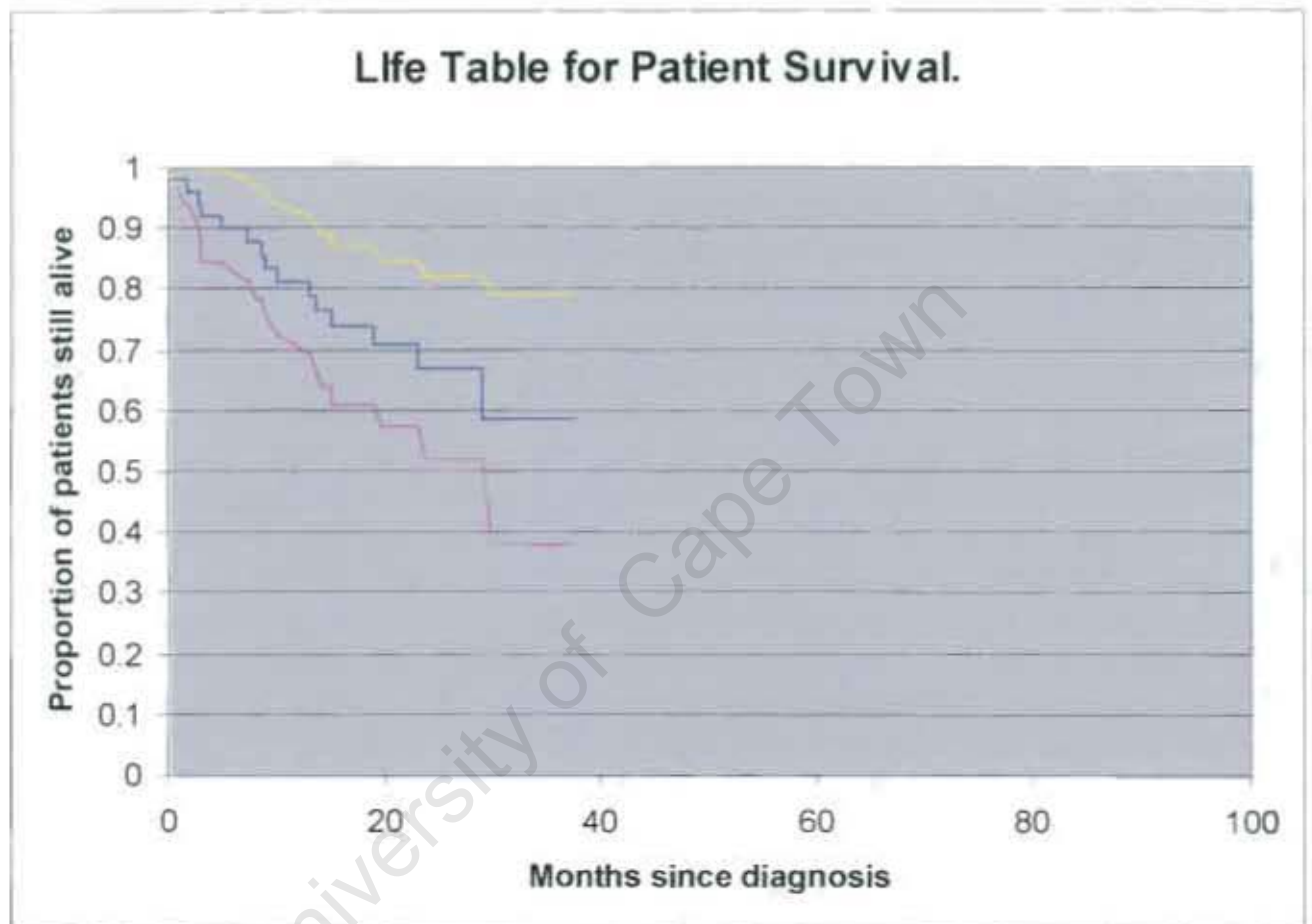
- 24 Patients attained a complete response to therapy. This means that all demonstrable disease had completely resolved when measured on 2 subsequent visits at least one month apart with no evidence of new lesions.
- 15 Patients achieved a partial response. This is defined as all measurable and evaluable disease decreasing by at least 50% on two separate occasions at least one month apart with no evidence of new lesions.
- 2 Patients had an improvement in disease status implying that the response was less than 50% and no new lesions present.
- 5 Patients had no change in their disease status.
- 5 Patients had progressive disease as their main response. This occurs if there is at least a 30% increase in size of measurable disease or the appearance of any new tumor lesions.

(v) **Survival**

The median survival time of all these patients was 86 months and the mean survival time was 64 months. After truncating the graph at 40 months, which is reasonable given that there were only 6 individuals still alive, no median survival could be estimated. (Graph I).

- No significant differences in survival could be shown for any particular subgroup of "Response to therapy".

Graph I    **Survival of all Patients**



- Actual Survival
- Confidence Interval
- Confidence Interval

(v) **VAD Complications**

Of the 54 VADs inserted the following complications were encountered:

1. 7 Fractures : All the fractures were at the connection of the VAD to the reservoir. In all cases the VADs were removed successfully. The broken VAD lines were also removed successfully, either by "snaring" them with a guide-wire passed through the femoral vein into the inferior vena cava and right atrium (6) or through sternotomy and cardiectomy (1).
2. Sepsis: Both cases had Gram positive cocci cultured in their blood. These were Coagulase negative Staphylococci.
3. 1 Too shallow with erosion through the skin of the chest wall.
4. 1 Tilt with resultant inability to insert the needle.
5. 1 Hemothorax at time of insertion.
6. 1 Jugular vein thrombosis occurring long after insertion.

Total: 13

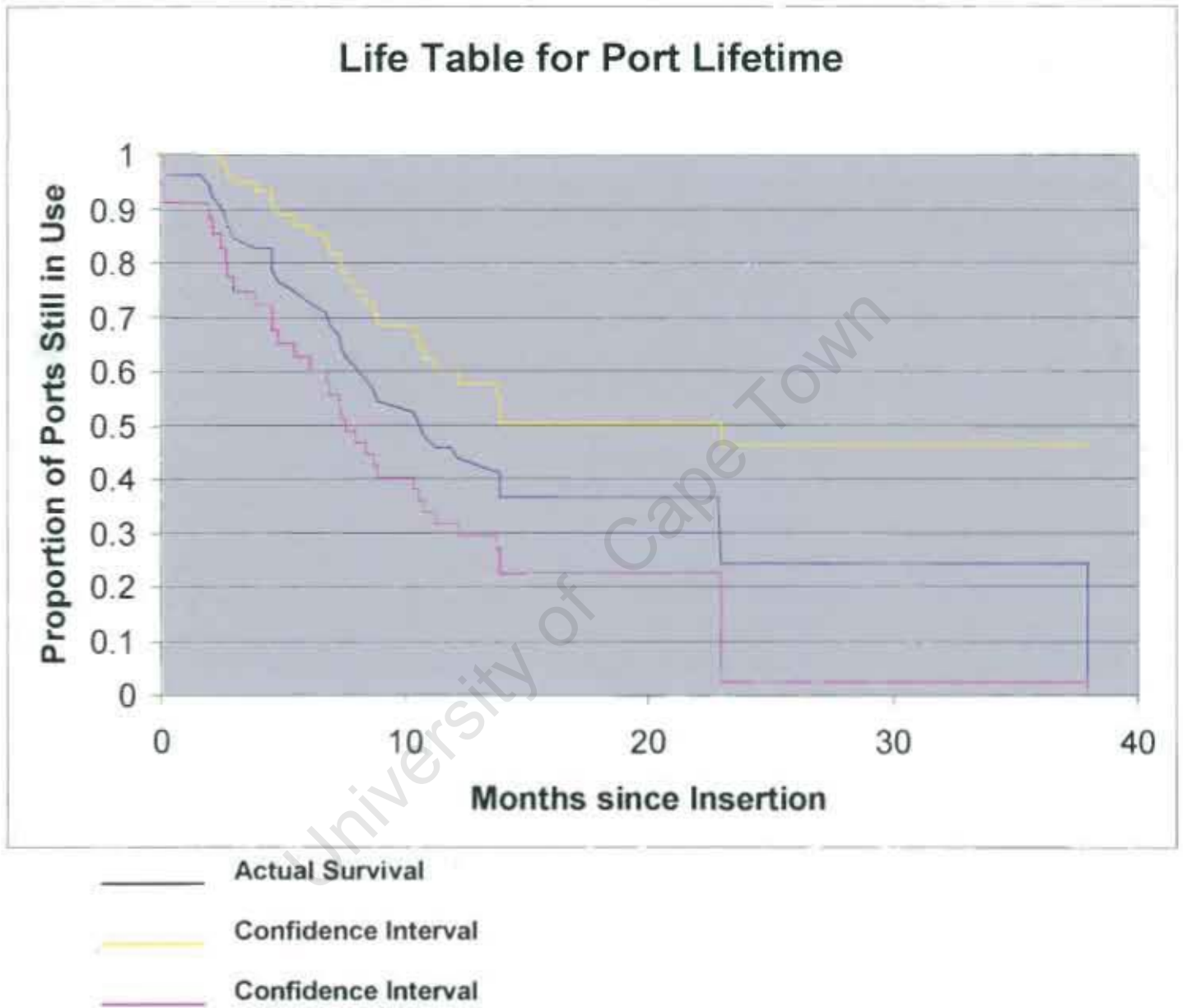
All these necessitated removal of the VAD.



(vi) **At The Time Of Analysis:**

- 22 patients had their VAD in situ for a mean of 15.7 months (1.2 – 38).
- 14 Patients had died and their VAD had not been removed. The mean duration of VAD-in-situ was 7.4 months (2.1 – 23).
- 18 VADs were inserted and then removed after a mean duration of 7.5 months (0.1 – 13.9). 5 VADs were removed as the patients had completed their therapy and 13 VADs were removed due to a complication.
- For all the VADs, the median "port survival" was 10.57 months. (See Graph II).

GRAPH II



### **Quality of Life Assessment**

Table II shows the results of multivariate tests performed on the EORTC-QLQ-C30 sub-scales. All functional scales, symptom scales and global health and quality of life scale were chosen as well as the additional symptom scale.

A comparison of the points in time for each sub-scale gave the following results:

1. Improvement of symptoms was significant as time progressed for fatigue ( $p = 0,005$ ), nausea ( $p = 0,02$ ), appetite ( $p = 0,04$ ), insomnia ( $p = 0,048$ ) with the least symptoms experienced in Time 3 i.e. the furthest time from baseline.
2. Although not significant, financial ( $p = 0,08$ ), constipation ( $p = 0,188$ ), also followed a similar trend with less symptoms being present at the furthest time from baseline.
3. For the functional sub-scales, a deterioration in functioning was present at the time of VAD placement and up to 53 days thereafter for the following: Cognitive ( $p=0,045$ ), role ( $p=0,069$ ), social ( $p=0,05$ ).

4. For both the Global healthy and quality of life scale ( $p=0,29$ ) and physical scale ( $p=0,65$ ), the highest (best) score was obtained the furthest time since VAD insertion (Time 3).
5. At time of the VAD insertion the following sub-scales showed the highest level of problems and lowest level of functioning. i) Cognitive, (ii) emotional, (iii) role (iv) social, (v) appetite, (vi) constipation, (vii) diarrhoea, (viii) dyspnoea, (ix) financial, (x) insomnia, (xi) nausea and emotional scale.

# Quality of Life Parameters

Table II

Variable	Den DF	F	Time	Score (0 – 100)	Pr>F (P-value)
Global Health (>)	8	1,84	Time 1 2 3	74,36 74 81	0,29
Cognitive (>)	8	4,66	Time 1 2 3	95,92 89,96 97,91	0,045
Emotional (>)	8	0,87	Time 1 2 3	86,48 79,07 84,2	0,45
Physical (>)	8	0,44	Time 1 2 3	89,96 90,3 92,57	0,65
Role (>)	8	3,79	Time 1 2 3	84,4 72,48 86,89	0,069
Social (>)	8	4,18	Time 1 2 3	85,08 73,74 88,32	0,05
Appetite (<)	8	4,65	Time 1 2 3	17 23 7	0,04
Constipation (<)	8	2,07	Time 1 2 3	9,28 9,77 2,69	0,188
Diarrhoea (<)	8	0,36	Time 1 2 3	3,96 6,11 3,36	0,7
Dyspnoea (<)	8	5,47	Time 1 2 3	17 22 7,4	0,03
Fatigue (<)	8	10,81	Time 1 2 3	29,48 29,37 13,02	0,005
Financial (<)	8	3,38	Time 1 2 3	13 18 7,4	0,08
Insomnia (<)	8	4,52	Time 1 2 3	17 26,96 10,10	0,048
Nausea (<)	8	6,2	Time 1 2 3	9,7 18,8 3,69	0,02

Scale Orientation: ">" - a higher score represents better functioning

"<" - a higher score represents a higher level of problems

Den DF = Denominator degrees of freedom

F = Test Statistic

P value = Probability value

## **FINANCIAL COST**

**Table 3** The costs in rands associated with VAD insertion, removal and monthly "flushing". The insertion of a VAD requires the following procedures financially costed out as follows:

1.	Cost of VAD	R1500.00
2.	Surgeon's fee	640.00
3.	Anaesthetist	550.00
4.	Radiology	370.00
5.	Hospital fee including ward, theatre	7000.00

**Total: R9060.00**

The removal of a VAD:

1.	Surgeon's fee	R300.00
2.	Anaesthetist	400.00
3.	Hospital fee, including ward, & theatre	3000.00

**Total: R3700.00**

The cost of "flushing a port" performed every time blood is withdrawn includes items:

1.	Whin needle	R28.00
2.	Dressing pack	15.39
3.	Heparin	23.52
4.	Gloves	7.27
5.	Primapore	6.36
6.	Syringe (5 ml)	4.62

**Total: R85.16**

Venous accessing costs were estimated in November 2003.

## **DISCUSSION**

This study evaluated information on the patients seen and treated at a single institution who were 21 years or younger and who had the diagnosis of cancer. All of these patients had VADs inserted to facilitate ease of administration of therapy as it was assumed that by inserting a VAD, the patient's quality of life would be improved.

The incidence of the diseases of the patients who were evaluated, was biased in that most adolescent and paediatric patients with haematological diseases and neoplasms are seen at other specialized academic units in government hospitals. The Mary Potter Oncology Center has a reputation for treating adolescents with sarcomas and is therefore a major centre of referral in Gauteng. The incidence rates of malignancy in these age groups, as reported for South Africa, is at variance with those reported for the USA and UK. This may in part be explained by under-reporting of tumors that occurs in South Africa.

Clinical trials to evaluate safety and efficacy of VADs have been single arm

Phase II studies : (i) Gyves J, et al, 1982;

(ii) Becton DL, et al, 1988

(iii) Strum S, et al, 1986

Or: Non-randomized studies: (i) Ingram J, et al, 1991

(ii) Stanislav G, et al, 1987

Or: Randomized studies: (i) Carde P, et al, 1989

(ii) Kappers-Klunne MC, et al, 1989

A number of authors have described the clinical complications associated with VADs, the most important being infection, although mechanical problems such as thrombosis are also frequent. In a retrospective review of 645 port systems a complication rate of (8,4%) was reported, with the common complications being infection (58%) and thrombosis (22%) and cases of port fracture (5,5%) (Chevral JP, 1996). In another series (Ingram J, 1991), of 144 subcutaneous ports, 46 (32%) were removed. The main complications were infection (4%), occlusion (1,4%), inadvertent needle dislodgement (1,4%), catheter rupture (1,4%), and mechanical occlusion (0,7%). In a further series (O'Neill, 1999), 110 Hickman catheters were inserted in 94 patients with solid tumors undergoing treatment with chemotherapy. Early complications included pneumothorax (4%), arterial puncture (1%), failure of placement (1%). Late complications included sepsis (24,5%), thrombosis (9%), line displacement (10%), and catheter blockage (1%). In the first randomized controlled trial which compared the use of totally implantable venous access devices before chemotherapy with standard peripheral venous access (Bow EJ, 1999), only 2 of 119



assessable patients crossed from VAD to peripheral line access because of VAD occlusion and catheter fracture.

In our series of 54 VADs, the major complications were a 'port fracture' in 7 VADs (13%), and sepsis with gram positive cocci (coagulase negative Staphylococci) in only 2 VADs (3,7%). The majority of the fractures occurred after long term use of the VAD and usually once the treatment had finished. No consistent problem with technique insertion could be determined. As the VADs were inserted by a number of different surgeons, no operator problem could be identified either. The broken catheter tips have been sent back to the manufacturers for assessment of the material used.

The quality of life parameters used represent a wide spectrum of the patient's life. The QLQ-C 30 was initially tested for validity based on comparisons between patient subgroup who were known to differ in clinical status. The QLQ-C 30 was less successful in discriminating between patients with different stages of disease, but was clearly able to distinguish between patients differing in terms of performance status, weight loss and treatment toxicity. An essential property of a quality of life instrument intended for use in the clinic is that it be responsive to changes in patients' health status over time. The QLQ-C 30 has shown statistically significant

changes in functional and symptom levels in the expected direction for patients whose performance status has either improved or deteriorated and no shifts in QLQ-C 30 scores were observed for those patients whose performance status remain unchanged over time (Aaronson NK, 1993). The present study demonstrates a trend to decrease in functional and well as symptom scores in the period of VAD insertion and up to 53 days post insertion. The most significant deterioration of score in the time period being cognitive, role and social functioning. There is evidence that chemotherapy per se can affect brain biochemistry directly, which results in mood disturbance and other cognitive impairment (Silberfarb 1980). It is possible then that patients who received chemotherapy within the same time frame as having the VAD inserted did have a decrease in their cognitive and other functioning, due to in part, by the chemotherapy. The scale assessing role functioning is amongst the briefest scales within the QLQ-C 30 and has the most restricted range of responses. Also the content area covered is limited to work and household activities and no leisure time activities are included. For younger patients the applicability of this limited range may not be a true reflection of what their role functioning really is, as the assessment may lack the necessary questions to truly assess an adolescent's role functioning. In the QOL study in-patients who had either VAD or peripheral lines (Bow EJ, 1999), QOL studies were performed to examine whether VAD use could influence functional quality of life. The instrument used was

the FLI-C (Clinch JJ, 1996). Although the VAD use reduced the venous access trauma and discomfort, no measurable improvement in quality of life attributable to the VAD could be demonstrated. It is important to remember that patients with cancer have special medical and psychiatric concerns, including fear of termination of treatment, pre-occupation with disease recurrence and minor physical problems and a sense of greater vulnerability to illness (Damocles syndrome). Also a pervasive awareness of mortality and difficulty with re-entry into normal life (the Lazarus syndrome). All of these fears have a profound influence on quality of life. Adolescents who have been treated for cancer not only have substantial physical, cognitive, emotional and interpersonal tasks faced by all adolescents but have the added burden of a life threatening disease. Persistent body image concerns, somatic-preoccupation, disruptions in sexual relationships and deficits in social competence are not uncommon (Mulhern R, Wasserman A, 1989). All of these factors have a profound influence on the adolescent and his/her functioning in all spheres and therefore would all affect the quality of life evaluation.

The financial costs involved have been studied and estimated in other studies (Bow EJ, 1999). Although it is impossible to assign a monetary value to human suffering related to vascular access problems, the reported average cost of accessing and maintaining a VAD for approximately 7

months in patients with cancer is \$2000. This represents over a billion dollars spent per year on VAD, in the USA. This is a conservative estimate as the projection does not take into account the costs of other access devices that have a higher complication rate and patients who require longer or more intensive chemotherapy (Freytes CO, 1999). This present study also under-estimated the costs in that the nursing time needed for flushing was not accounted for. Neither the extra costs of removing a fractured line of the VAD nor the additional antibiotics, fibrinolytics and anti-coagulants needed to treat the complications have been included in the calculation.

## **CONCLUSION**

The evaluated quality of life scores in the patients who had VADs inserted to facilitate administration of treatment show a decrease in most parameters at the time of the VAD insertion and up to 53 days thereafter. This is then followed by an increase in QOL parameters to over and above the initial levels. Results from studies of adolescents with cancer show that there are long-term survivors. Complication rates due to VAD use are not particularly high, and the initial deterioration in QOL scores are temporary. The prime advantages of having a VAD are the convenience of ease of administration of treatment, convenience and safety of the venous access.

Future studies should evaluate the teenagers QOL with more specific questionnaires relating to an adolescents QOL. Only then can an honest argument be presented to a patient to allow for an informed decision to be made regarding insertion of a VAD.

## REFERENCES

Aaronson NK, Ahmedzar S, Bergman B et al. The European Organization for Research and Treatment of Cancer QLQ-C-30. A quality of life instrument for use in international clinical trials in oncology. J. Natl. Cancer Instit. 85: 365-376, 1993.

Alhimyary A, Fernandez C, Picard M et al. Safety and efficacy of total parenteral nutrition delivered via a peripherally inserted central venous catheter. Nutr. Clin. Pract. 1996;11:199.

Anderson KM, Holland JS. Maintaining the patency of peripherally inserted central catheters with 10 units/cc Heparin. J. Intraven. Nurs. 1992; 15: 84.

Banton J. Using midlines and PICC lines for chemotherapy regimes. Oncol Nurs. Forum 1999: 26:514.

Barr R. On cancer control and the adolescent. Med Pediatr Oncol. 1999: 32:404-10.

Becton DL, Kletzel M, Gollady ES, et al: An experience with an implanted port system in 66 children with cancer. Cancer 61: 376-378, 1988.

Bottino J, McCredie KB, Groschel DHM, Lauson M. Longterm intravenous therapeutic peripherally inserted silicone elastomer central venous catheters in patients with malignant disease. *Cancer* 1979;43:1937.

Bow EJ, Kilpatrick MG, Clinch JJ: Totally Implantable Venous Access Ports Systems for Patients receiving Chemotherapy for Solid Tissue Malignancies: A Randomized Controlled Clinical Trial Examining the Safety, Efficacy, Costs, and Impact on Quality of Life. *J Clin Oncol*, Vol 17:4, April 1999.

Broviac JW, Cole JJ, Scribner BH. A silicone rubber atrial catheter for prolonged parenteral alimentation. *Surg. Gynecol. Obstet.* 1973; 136:602.

Carde P, Cosset-Delaigue MF, LaPlanche A et al: Classical external indwelling central venous catheter versus totally implanted venous access systems for chemotherapy administration. A randomized trial in 100 patients with solid tumours. *Eur J Clin Oncol* 25: 939-944, 1989.

Chevral JP, Breau, JL, Zhang J. Long-term results of an Implantable Port System – A Retrospective Review. Personal File. Celsa, France, Poitiers, 1996.

Clinch JJ: The Functional Living Index – Cancer. Ten years later, in Spilker B.(ed). Quality of life and Pharmaco-economics in Clinical Trials (ed 2). Philadelphia PA, Lippincott –Raven, 1996 pp 215-225).

Decker MD, Edwards KM. Central venous catheter infections. Paediatr. Clin. North Am. 1988: 35:579.

Evans M. Interacting with teenagers with cancer. In: Selby P, Bailey C, Cancer and the adolescent. London BMJ Publishing Group, 1996: 251-63.

Festa RS, Tamaroff MH, Chasalow F et al. Therapeutic adherence to oral medication regimens by adolescents with cancer. In Laboratory Assessment. J Pediatr 1992: 120: 807-811.

Freytes CO. Vascular Access investigation comes of age. Support Care Cancer 1999, 7: 373-374.

Goodman MS, Wickham R: Venous access devices: an oncology nurse overview. Hosp. Pharm. 20:495, 1985.



Gyves J, Ensminger W, Niederhuber J: Totally implantable system for intravenous chemotherapy in patients with cancer. *Am J Med* 73: 841-846, 1982.

Hickman RO, Buckner CD, Clift RA et al. A modified right atrial catheter for access to the venous system in marrow transplant recipients. *Surg. Gynecol. Obstet.* 1979; 148:871.

Ingram J, Weitzman S, Greenberg M, et al. Complications of Indwelling venous access lines in the Paediatric Hematology patient. A prospective comparison of external venous catheters and subcutaneous ports. *The American Journal of Pediatric Hematology/Oncology* 13(2): 130-136, 1991.

James L, Bledsoe L, Hadawaz LC. A retrospective look at tip location and complications of peripherally inserted central catheter lines. *J. Intraven. Nurs.* 1993; 16:104.

Kaplan E L, Meier P. Nonparametric estimations of incomplete observations. *J. Amer. Stat. Assoc.* 53: 457- 481, 1958.

Kappers-Klunne MC, Degener JE, Stijnen T, et al: Complications from long-term indwelling central venous catheters in haematologic patients with special reference to infection. *Cancer* 64: 1747-1752, 1989.

Kosary CL, Ries LAG, Miller BA et al SEER. *Cancer Statistics Review* 1973-1992. Tables and Graphs HHS public. No 96-2789 Bethesda MD National Cancer Institute 1995.

Leonard R, Coleman R, Gregar A et al. Special problems of adolescents with cancer. *J Cancer Care* 1995; 5: 117-20.

Lucas AB. A critical review of venous access devices: the nursing perspective. *Curr. Issues Cancer Nurs. Pract.* 1992: 1:1.

Mirro J, Rao BN, Kumar M et al. A comparison of placement techniques and complications of externalized catheters and implantable port use in children with cancer. *J. Pediatr. Surg.* 1990: 25: 120.

Mqoqi N, Kellett P, Madhoo J, Sitas F. Incidence of Histologically Diagnosed Cancer in South Africa 1996 –1997.

Mulhern R, Wasserman A, Friedman A, Fairclough D. Social competence and behavioral adjustment in children who are long-term survivors of cancer. *Pediatrics* 1989, 83, 18.

Niederhuber JE, Enslinger N, Gyves JW et al. Totally implanted venous and arterial access system to replace external catheters in cancer treatment. *Surgery* 1982;92:706.

Parkin, DM, Muir CS, Whelan S et al eds. Cancer incidence in five continents Vol 6, Lyon IARC. Scientific Publication 1992.

Press OW, Ramsey PG, Larson EB et al. Hickman catheter infections in patients with malignancies. *Medicine* 1984: 63:189.

Ries LAG, Smith MA, Gurney JG, et al eds. Cancer Incidence and Survival among children and Adolescents. United States SEER program 1975-1995. NIH Pub No 99-9649, Bethesda, MD. National Cancer Institute SEER Program 1999.

Silberfarb PM, Philibert D, Levine PM, 1980. Psycho-social aspects of neoplastic disease II. Affective and cognitive effects of chemotherapy in cancer patients. *Am J. Psychiatry* 137: 597-601.

Stanislav G, Fitzgibbons RJ, Jnr, Bailey RT et al: Reliability of implantable central venous access devices in patients with cancer. *Arch. Surg.* 122: 1280 – 1283, 1987.

Strom S, McDermid J, Korn A et al: Improved methods for venous access. The Port-a –Cath, a totally implanted catheter system. *J. Clin. Oncol.* 4: 596-603, 1986.

Stuart A, Ord J K – 1991 Kendall's advanced theory of Statistics. 5<sup>th</sup> Edition. Vol 2, Chap 29. Edward Arnold, Ldn.

Stiller CA, McKinney PA, Bunch KJ, Bailey CC, Lewis LL. Childhood cancer and ethnic group in Britain. A United Kingdom Children's Cancer Study Group study. *Br. J. Cancer* 1991: 64, 545-548.

Vincent J. O'Neill TR, Jeffrey Evans, Janice Preston, John Moss, Stanley B Kaye. A retrospective Analysis of Hickman Line-Associated Complications in Patients with Solid Tumors undergoing Infusional Chemotherapy. *Acta Oncologica* Vol 38, No 8, pp 1103 – 1107, 1999.

Ware JE Jr., Brook RH, Davies-Avery A et al. Conceptualization and Measurement of Health of Adults in the Health Insurance Study. Vol 1: Model of Health and Methodology. Santa Monica, Calif: Rand Corporation, 1980.

Woo SY, Sinks LF. Neoplastic diseases. In: Adolescent medicine: morbidity and mortality. Shearin R. editor. GK Hall and Company. 1983, p97-115.

Wurzel CL, Halom K, Feldman JG, Rubin LG. Infection rates of Brovac-Hickman catheters and implantable venous devices. *Am. J. Dis. Child.* 1988;142:536.